

Amendment to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-47. (canceled)

48. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 or the full length complementary sequence thereof.

49-50. (canceled)

51. (previously presented) An expression vector comprising the isolated nucleic acid of claim 48 and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO:43.

52. (original) The recombinant expression vector of claim 51, wherein said vector is suitable for transfection of a bacterial cell.

53. (previously presented) An isolated cell transfected with the vector of claim 51, wherein said cell expresses the β -secretase consisting of SEQ ID NO:43.

54. (original) The cell of claim 53, wherein said cell is a eukaryotic cell.

55. (original) The cell of claim 53, wherein said cell is a bacterial cell.

56. (original) The cell of claim 53, wherein said cell is an insect cell.

57. (original) The cell of claim 53, wherein said cell is a yeast cell.

58. (currently amended) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO: 43, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43 or under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

59. (original) The method of claim 58, wherein said affinity matrix contains a β -secretase inhibitor molecule.

60. (previously presented) The method of claim 59, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

61. (original) The method of claim 58, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

62-63. (canceled)

64. (previously presented) An isolated cell, comprising

(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 43;

(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

65-66. (canceled)

67. (previously presented) The cell of claim 64, wherein said β -secretase substrate molecule is selected from the group consisting of human wild type amyloid precursor protein (APPwt), a beta-secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, the Swedish mutation of APPwt (APPsw), and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO:51.

68. (currently amended) The cell of claim 64, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~ protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw).

69. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 82.

70-113. (canceled)

114. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 58 or the full length complementary sequence thereof.

115. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 114 and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 58.

116. (previously presented) The expression vector of claim 115, wherein said vector is suitable for transfection of a bacterial cell.

117. (previously presented) An isolated cell transfected with the vector of claim 115, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 58.

118. (previously presented) The cell of claim 117, wherein said cell is a eukaryotic cell.

119. (previously presented) The cell of claim 117, wherein said cell is a bacterial cell.

120. (previously presented) The cell of claim 117, wherein said cell is an insect cell.

121. (previously presented) The cell of claim 117, wherein said cell is a yeast cell.

122. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 59 or the full length complementary sequence thereof.

123. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 122 and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 59.

124. (previously presented) The expression vector of claim 123, wherein said vector is suitable for transfection of a bacterial cell.

125. (previously presented) An isolated cell transfected with the vector of claim 123, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 59.

126. (previously presented) The cell of claim 125, wherein said cell is a eukaryotic cell.

127. (currently amended) The cell of ~~claim~~ claim 125, wherein said cell is a bacterial cell.

128. (previously presented) The cell of claim 125, wherein said cell is an insect cell.

129. (previously presented) The cell of claim 125, wherein said cell is a yeast cell.

130. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 66 or the full length complementary sequence thereof.

131. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 130 and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 66.

132. (previously presented) The expression vector of claim 131, wherein said vector is suitable for transfection of a bacterial cell.

133. (currently amended) An isolated cell transfected with the vector of claim 131 ~~claim 130~~, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 66.

134. (previously presented) The cell of claim 133, wherein said cell is a eukaryotic cell.

135. (previously presented) The cell of claim 133, wherein said cell is a bacterial cell.

136. (previously presented) The cell of claim 133, wherein said cell is an insect cell.

137. (previously presented) The cell of claim 133, wherein said cell is a yeast cell.

138. (currently amended) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 67 or the full length complementary sequence thereof.

139. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 138 and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 67.

140. (previously presented) The expression vector of claim 139, wherein said vector is suitable for transfection of a bacterial cell.

141. (previously presented) An isolated cell transfected with the vector of claim 139, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 67.
142. (previously presented) The cell of claim 141, wherein said cell is a eukaryotic cell.
143. (previously presented) The cell of claim 141, wherein said cell is a bacterial cell.
144. (previously presented) The cell of claim 141, wherein said cell is an insect cell.
145. (previously presented) The cell of claim 141, wherein said cell is a yeast cell.
146. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 68 or the full length complementary sequence thereof.
147. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 146, and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 68.
148. (previously presented) The expression vector of claim 147, wherein said vector is suitable for transfection of a bacterial cell.
149. (previously presented) An isolated cell transfected with the vector of claim 147, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 68.
150. (previously presented) The cell of claim 149, wherein said cell is a eukaryotic cell.
151. (previously presented) The cell of claim 149, wherein said cell is a bacterial cell.
152. (previously presented) The cell of claim 149, wherein said cell is an insect cell.
153. (previously presented) The cell of claim 149, wherein said cell is a yeast cell.

154. (previously presented) An isolated nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 69 or the full length complementary sequence thereof.

155. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 154, and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO:69.

156. (previously presented) The expression vector of claim 155, wherein said vector is suitable for transfection of a bacterial cell.

157. (previously presented) An isolated cell transfected with the vector of claim 155, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 69.

158. (previously presented) The cell of claim 157, wherein said cell is a eukaryotic cell.

159. (previously presented) The cell of claim 157, wherein said cell is a bacterial cell.

160. (previously presented) The cell of claim 157, wherein said cell is an insect cell.

161. (previously presented) The cell of claim 157, wherein said cell is a yeast cell.

162. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 70 or the full length complementary sequence thereof.

163. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 162, and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO:70.

164. (previously presented) The expression vector of claim 162, wherein said vector is suitable for transfection of a bacterial cell.

165. (previously presented) An isolated cell transfected with the vector of claim 163, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 70.

166. (previously presented) The cell of claim 165, wherein said cell is a eukaryotic cell.

167. (previously presented) The cell of claim 165, wherein said cell is a bacterial cell.

168. (previously presented) The cell of claim 165, wherein said cell is an insect cell.

169. (previously presented) The cell of claim 165, wherein said cell is a yeast cell.

170. (previously presented) An isolated nucleic acid encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 74 or the full length complementary sequence thereof.

171. (previously presented) An expression vector, comprising the isolated nucleic acid of claim 170, and a promoter, wherein the nucleic acid and the promoter are operably linked, and wherein the beta secretase produced by expressing said vector consists of SEQ ID NO: 74.

172. (previously presented) The expression vector of claim 171, wherein said vector is suitable for transfection of a bacterial cell.

173. (previously presented) An isolated cell transfected with the vector of claim 171, wherein said cell expresses the β -secretase consisting of SEQ ID NO: 74.

174. (previously presented) The cell of claim 173, wherein said cell is a eukaryotic cell.

175. (previously presented) The cell of claim 173, wherein said cell is a bacterial cell.

176. (previously presented) The cell of claim 173, wherein said cell is an insect cell.

177. (previously presented) The cell of claim 173, wherein said cell is a yeast cell.

178. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO: 58, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 58

under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

179. (previously presented) The method of claim 178, wherein said affinity matrix contains a β -secretase inhibitor molecule.

180. (previously presented) The method of claim 179, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

181. (previously presented) The method of claim 178, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

182-183. (canceled)

184. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO: 59, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 59 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

185. (previously presented) The method of claim 184, wherein said affinity matrix contains a β -secretase inhibitor molecule.

186. (previously presented) The method of claim 185, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

187. (previously presented) The method of claim 184, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

188-189. (canceled)

190. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO:66, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 66 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

191. (previously presented) The method of claim 190, wherein said affinity matrix contains a β -secretase inhibitor molecule.

192. (previously presented) The method of claim 191, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

193. (previously presented) The method of claim 190, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

194-195. (canceled)

196. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO:67, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:67 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

197. (previously presented) The method of claim 196, wherein said affinity matrix contains a β -secretase inhibitor molecule.

198. (previously presented) The method of claim 197, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

199. (previously presented) The method of claim 196, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

200-201. (canceled)

202. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO:68, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 68 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

203. (previously presented) The method of claim 202, wherein said affinity matrix contains a β -secretase inhibitor molecule.

204. (previously presented) The method of claim 203, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

205. (previously presented) The method of claim 202, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

206-207. (canceled)

208. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO:69, comprising culturing a cell transfected with a vector comprising a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:69 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

209. (previously presented) The method of claim 208, wherein said affinity matrix contains a β -secretase inhibitor molecule.

210. (previously presented) The method of claim 209, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

211. (previously presented) The method of claim 210, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

212-213. (canceled)

214. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO: 70, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 70 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

215. (previously presented) The method of claim 214, wherein said affinity matrix contains a β -secretase inhibitor molecule.

216. (previously presented) The method of claim 215, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

217. (previously presented) The method of claim 214, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

218-219. (canceled)

220. (previously presented) A method of producing a recombinant β -secretase enzyme consisting of SEQ ID NO: 74, comprising culturing a cell transfected with a vector comprising a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO: 74

under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.

221. (previously presented) The method of claim 220, wherein said affinity matrix contains a β -secretase inhibitor molecule.

222 (previously presented) The method of claim 221, wherein said inhibitor molecule is P10-P4'staD->V (SEQ ID NO:73).

223. (previously presented) The method of claim 220, wherein said matrix contains an antibody characterized by an ability to bind β -secretase.

224-225. (canceled)

226. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

227. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

228. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

229. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

230. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

231. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

232. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

233. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

234. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

235. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

236. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

237. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

238. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

239. (previously presented) The cell of claim 67, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

240. (previously presented) An isolated cell, comprising
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:58
(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

241-242. (canceled)

243. (previously presented) The cell of claim 240, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

244. (currently amended) The cell of claim 240, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

245. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

246. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

247. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

248. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

249. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

250. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

251. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

252. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

253. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

254. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

255. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

256. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

257. (previously presented) The cell claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

258. (previously presented) The cell of claim 243, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

259. (previously presented) An isolated cell, comprising
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:59;
(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

260-261. (canceled)

262. (previously presented) The cell of claim 259, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

263. (currently amended) The cell of claim 259, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~~~binding~~ protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

264. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

265. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

266. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

267. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

268. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

269. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

270. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

271. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

272. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

273. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

274. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

275. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

276. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

277. (previously presented) The cell of claim 262, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

278. (previously presented) An isolated cell, comprising

(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleic acid encoding a beta secretase, the nucleic acid consisting of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:66;

(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

279-280. (canceled)

281. (previously presented) The cell of claim 278, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO:54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO:51.

282. (currently amended) The cell of claim 278, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

283. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

284. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

285. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

286. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

287. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

288. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

289. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

290. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

291. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

292. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

293. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

294. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

295. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

296. (previously presented) The cell of claim 281, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

297. (previously presented) An isolated cell, comprising

(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:67;

(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

298-299. (canceled)

300. (previously presented) The cell of claim 297, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO:54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO:51.

301. (currently amended) The cell of claim 297, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

302. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

303. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

304. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

305. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

306. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

307. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

308. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

309. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

310. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

311. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

312. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

313. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

314. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

315. (previously presented) The cell of claim 300, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

316. (previously presented) An isolated cell, comprising
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:68;
(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

317-318. (canceled)

319. (previously presented) The cell of claim 316, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

320. (currently amended) The cell of claim 316, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binging protein having the c-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence

of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

321. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

322. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

323. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

324. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

325. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

326. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

327. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

328. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

329. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

330. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

331. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

332. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

333. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

334. (previously presented) The cell of claim 319, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

335. (previously presented) An isolated cell, comprising
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:69;
(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

336-337. (canceled)

338. (previously presented) The cell of claim 335, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

339. (currently amended) The cell of claim 335, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~~~binding~~ protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

340. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

341. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

342. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

343. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

344. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

345. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

346. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

347. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

348. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

349. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

350. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

351. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

352. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

353. (previously presented) The cell of claim 338, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

354. (previously presented) An isolated cell, comprising
(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:70;
(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and
(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

355-356. (canceled)

357. (previously presented) The cell of claim 354, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

358. (currently amended) The cell of claim 354, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

359. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

360. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

361. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

362. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

363. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

364. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

365. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

366. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

367. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

368. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

369. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

370. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

371. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

372. (previously presented) The cell of claim 357, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.

373. (previously presented) An isolated cell, comprising

(i) a nucleic acid molecule encoding a beta secretase, wherein the nucleic acid consists of a nucleotide sequence encoding the beta secretase consisting of SEQ ID NO:74;

(ii) a nucleic acid molecule encoding a β -secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

374-375. (canceled)

376. (previously presented) The cell of claim 373, wherein said β -secretase substrate molecule is selected from the group consisting of APPwt, a beta secretase cleavable fragment of APPwt comprising SEQ ID NO: 54, APPsw, and a β -secretase cleavable fragment of APPsw comprising SEQ ID NO: 51.

377. (currently amended) The cell of claim 373, wherein said β -secretase substrate is selected from the group consisting of a fusion protein of maltose ~~binding~~binding protein having the C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPwt, and a fusion protein of maltose binding protein having C-terminus fused to the N-terminus of the 125 amino acid carboxy-terminal sequence of APPsw.

378. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 83.

379. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 84.

380. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 85.

381. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 86.

382. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 87.

383. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 88.

384. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 89.

385. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 90.

386. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 91.

387. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 92.

388. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 93.

389. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 94.

390. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 95.

391. (previously presented) The cell of claim 376, wherein said β -secretase-cleavable fragment is SEQ ID NO: 96.